Dev Biol. 2004 Mar 15;267(1):14-28. Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Essential roles of Meltrin beta (ADAM19) in heart development.

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Morphogenesis of the heart requires development of the endocardial cushion tissue that gives rise to the membranous septa and valves. Here we show that Meltrin beta/ADAM19, a novel metalloprotease-disintegrin, participates in the development of the endocardial cushion. Mice lacking Meltrin beta exhibit ventricular septal defect (VSD) and immature valves, and most of the animals die soon after birth. During development of the endocardial cushion, epithelial-mesenchymal transformation (EMT) of endocardial epithelial cells generates most of the cushion mesenchymes that constitute the main components of the septa and valves. Meltrin beta is expressed in both the epithelia and the mesenchymes of the endocardial cushion. In the absence of Meltrin beta, the cushion is small or thin in the septum-forming region and show poor remodeling of cardiac jelly components; both of these characteristics suggest impaired growth and differentiation of the endocardial cushion. When embryonic fibroblasts are cultured sparsely, Meltrin beta-lacking cells exhibit aberrant ectodomain shedding of type I Neuregulin, one of the ErbB ligands expressed in endocardial cells. These results suggest the necessity of proteolytic regulation of ErbB ligands by Meltrin beta for proper heart development.

PMID: 14975714 [PubMed - in process]